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| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/665,111 | SCHENDEL ET AL. | |
| | Examiner | Art Unit | |
| | Karen A. Canella | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *23-30 and 32-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-25,27-30,32-34 and 37-49* is/are rejected.

7)☒ Claim(s) *26, 35 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Claims 23, 27 and 33 have been amended. Claims 47-49 have been added. Claims 23-30, 32-49 are pending and under consideration.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-30, 32, 43 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A)The recitation of "the patient" in claim 27 lacks specific antecedent basis within the claim.

(B) Claim 48 recites the "method according to claim 27", however, claim 27 is drawn to a product, not a method. For purpose of examination, claim 48 will be read as the composition of claim 27.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 27, 28, 30, 32, 43 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Philip et al (Cancer Gene Therapy, 1998, Vol. 5, pp. 236-246).

Clam 27 is drawn to a pharmaceutical composition comprising antigen-presenting cells into which protein and or peptide or RNA or DNA or cDNA encoding said proteins and/or peptides have been introduced, wherein the APC are semi-allogeneic and HLA-haploidentical with respect to those of the patient, wherein the HLA-haploidentical APC have class I and class II molecules in common with the patient and wherein said proteins and/or peptides are over expressed in tumor cells of a patient with a tumor disease or are derived from tumor cells from the patient. Claim 28 embodies the composition of claim 27, wherein the proteins, peptides, RNA or DNA or cDNA encoding said proteins or peptide are selected from carcinomas, hematopoietic tumor cells, mesenchymal tumor cells, epithelial tumor cells, ectodermal tumor cells, and embryonic tumor cells from undifferentiated tissue. Claim 30 embodies the composition of claim 27 wherein the HLA-haploidentical APC are dendritic cells or macrophages. Claim 32 embodies the composition of claim 27 that is a vaccine. Claim 43 embodies the composition of claim 28 wherein the carcinomas are ovarian, mammary and renal, the hematopoietic cells are leukemias and lymphomas, the mesenchymal tumor cells are sarcomas, the ectodermal tumors are melanomas and the embryonic tumors are blastomas and teratomas. Claim 47 embodies the composition of claim 23, wherein the HLA-haploidentical APC of the donor have a HLA-haplotype that is 50% identical to that of the patient.

It is noted that claims 27, 28, 30, 32, 43 and 47 are drawn to a composition. Thus, the recitation of "the patient" in claim 27 implies an intended use for said composition which does not provide patentable weight when distinguishing the claim from the prior art.

Philip et al disclose the expression of MART-1 cDNA in human dendritic cells prepared from healthy individuals as well as peptide-loaded dendritic cells (page 237 under “Preparation of DC”, “Plasmid constructs and preparation”, page 238 under “Peptide-loaded DC). The dendritic cells of Philip et al meets the specific embodiments of the instant claims because they are inherently "haploidentical" to an appropriate recipient and possess an HLA-haplotype 50% identical to an appropriate recipient. Furthermore, the MART-1 antigen is over expressed in melanoma, which meets” the limitations of claims 28 and 43.

Claims 27, 28, 30, 32, 43 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Song et al (U.S. 2002/0123479).

Song et al disclose dendritic cells comprising an expression vector which direct expression of antigens associated with cancers, including breast, colon, and brain cancer, melanoma and leukemias (paragraph [0007] and paragraph [[0010]. Song et al disclose a method of treatment of cancer (paragraph [0006]) comprising the administration of a dendritic cell population transduced ex vivo (paragraph [0017]).

The ex vivo transduced dendritic cells of Song et al meets the specific embodiments of the instant claims because they are inherently "haploidentical" to an appropriate recipient and possess an HLA-haplotype 50% identical to an appropriate recipient.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27-30, 32, 43 and 47 rejected under 35 U.S.C. 103(a) as being unpatentable over Philip et al (Cancer Gene therapy, 1998, Vol. 5, pp. 236-246) in view of Cohen (WO98/33527, cited in a prior action) and Warnier et al (WO 98/58956, cited in a prior action).

Claim 29 embodies the composition of claim 27 wherein the proteins, peptides, RNA, DNA, or cDNA are derived from several different tumor cell lines.

Cohen et al teach the incorporation of DNA or RNA encoding for at least one tumor antigen introduced into an antigen presenting cell (page 30, lines 1-3 and 7-8) as well as the

transduction of tumor genomic DNA obtained from a tumor cell line (page 8, lines 8-11 and page 30, lines 11-16). Cohen does not specifically teach using polynucleotides or polypeptides from several different tumor cell lines, although Cohen et al does teach using "at least one" tumor antigen which is suggestive of using multiple tumor antigens.

Warnier et al teach that tumors express a set of tumor antigens, of which only certain subsets may be expressed in the tumor of any given patient and the desirability of having antigen-presenting cells expressing "polytopes" comprising multiple epitopes on tumor antigens in order to reflect a boarder spectrum of tumor associated antigens (page 20, line 31 to page 21, line 7)

It would have been prima facie obvious at the time the clamed invention was made to pulse or transduce the dendritic cells of Philip et al using peptides or cDNA from more than one tumor cell line. One of skill in the art would have been motivated to do so by the teachings of Cohen et al on the incorporation of DNA or RNA encoding at least one tumor antigen introduced into an APC from "at least one" tumor cell line which is suggestive of more than one cell line and the teachings of Warnier et al on the restricted expression of antigen on patient tumors. One of skill in the art would have been motivated to include the antigens from several different tumor cell lines in order to insure that the antigen–presenting cell would provide antigens which were expressed on actual patient tumors.

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Claims 23, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al in view of Wong et al (WO96/04314).

Song et al teach dendritic cells comprising an expression vector which direct expression of antigens associated with cancers, including breast, colon, and brain cancer, melanoma and leukemias (paragraph [0007] and paragraph [[0010]. Song et al teach a method of treatment of cancer (paragraph [0006]) comprising the administration of a dendritic cell population transduced ex vivo (paragraph [0017]). Song et al teach expression vectors encoding a "gene of interest" such as Rb, p53, ras, DCC, MCC and mucin (paragraph [0048]) which meets the limitation of claims 39 and 45. Song et al teach that ex vivo transduced monocytes/macrophages and dendritic cells are excellent sources for transferring immune responses (paragraph [0184]). Song et al teach that the dendritic cells can be administered by intravenous of subcutaneous

routes (paragraph [0017]) which meets the limitations of claim 37. Song et al suggest that haplotype-matched, transduced dendritic or monocytes/macrophages may be used as an immunotherapeutic approach to disease treatment (paragraph [0184]). Song et al does not specifically teach that haplotype-matched transduced dendritic cells are administered for the treatment of cancer in a subject.

Wong et al teach that host-compatible antigen-presenting cells into which recombinant DNA is introduced may be administered to a subject (page 35, lines 9-11). Wong et al teach that as recognized in the art, "host compatible" antigen presenting cells means APCs that are of the same haplotype of the subject or "host" to which the cells are administered (page 36, lines 3-7).

It would have been prima facie obvious at the time that the claimed invention was made to administer the haplotype-matched dendridic cells of Song et al for the treatment of cancer in a subject. One of skill in the art would have been motivated to do so by the suggestion of Song et al that transduced, haplotype-matched dendritic cells be used in immunotherapy, and the teachings of Wong et al on the administration of antigen presenting cells expressing a recombinant protein to a subject. wherein said APC are of the same haplotype as the subject.

Claims 23, 25, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al and Wong et al as applied to claims 23, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 above, and further in view of Eastman et al (WO 01/36680, cited in a prior action) and Schuller et al (WO 02/36790, cited in a prior action).

Claim 25 embodies the method of claim 23 wherein the first RNA from tumor cells cDNA, the cDNA is amplified by RCR and transcribed into RNA.

Eastman et al teach a method for preparing cRNA comprising amplification of cDNA (claim 3).

Schuller et al teach a method of infected dendritic cells with influenza virus vector wherein said vector incorporates RNA (claims 1, 11 and 12 and page 19, lines 28-30).

It would have been prima facie obvious to substitute the influenza viral vector of Schuller et al comprising RNA obtained by reverse transcribing cDNA as taught by Eastman et al in the method and products rendered obvious by the combination of Song et al and Wong et al.. One of skill in the art would have been motivated to dos o by the teachings of Schuller et al on the

transfection of dendritic cells with the influenza virus vector which incorporates RNA and the teachings of Eastman et al on the method of making cRNA, which would provide the RNA for incorporation into said vector.

Claims 23, 24, 27, 28, 29, 30, 32-34 and 37-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al and Wong et al as applied to claims 23, 27, 28, 30, 32, 33, 34, 37-40, 43-45 and 47-49 above, and further in view of Cohen (WO98/33527) and Warnier et al (WO 98/58956)

Cohen et al teach the incorporation of DNA or RNA encoding for at least one tumor antigen introduced into an antigen presenting cell (page 30, lines 1-3 and 7-8) as well as the transduction of tumor genomic DNA obtained from a tumor cell line (page 8, lines 8-11 and page 30, lines 11-16). Cohen does not specifically teach using polynucleotides or polypeptides from several different tumor cell lines, although Cohen et al does teach using "at least one" tumor antigen which is suggestive of using multiple tumor antigens. Cohen teaches that coding sequences for specific tumor antigens expressed in the tumor to be treated can be introduced into the semi-allogeneic APC of the invention, and that said coding sequences include the genes for Muc-1 and Her-2 (page 27, line 26 to page 28, line 14)

Warnier et al teach that tumors express a set of tumor antigens, of which only certain subsets may be expressed in the tumor of any given patient and the desirability of having antigen-presenting cells expressing "polytopes" comprising multiple epitopes on tumor antigens in order to reflect a boarder spectrum of tumor associated antigens (page 20, line 31 to page 21, line 7)

It would have been prima facie obvious at the time the clamed invention was made to transduce the dendritic cells of Song et al using peptides or cDNA from more than one tumor cell line or the tumor defined antigen of Her-2 or Muc1, and administer said dendritic cells to a subject for the treatment of cancer. One of skill in the art would have been motivated to do so by the teachings of Cohen et al on the incorporation of DNA or RNA encoding at least one tumor antigen introduced into an APC from "at least one" tumor cell line which is suggestive of more than one cell line and the teachings of Warnier et al on the restricted expression of antigen on patient tumors. One of skill in the art would have been motivated to include the antigens from

several different tumor cell lines in order to insure that the antigen–presenting cell would provide antigens which were expressed on actual patient tumors. One of skill in the art would also have been motivated to include the tumor defined antigens of Her-2 or Muc-1 in recombinant dendritic cells to be administered subjects with tumors expressing Her-2 or Muc1, because Cohen suggests these alternatives for cancer treatment.

Claims 26, 35 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

All other rejections and objections as set forth or maintained in the prior Office action are withdrawn in light of applicant's arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/

Primary Examiner, Art Unit 1643